



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2021-D-0241]

Inspection of Injectable Products for Visible Particulates; Draft Guidance for Industry;
Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Inspection of Injectable Products for Visible Particulates.” Visible particulates in injectable products can jeopardize patient safety. This draft guidance addresses the development and implementation of a holistic, risk-based approach to visible particulate control that incorporates product development, manufacturing controls, visual inspection techniques, particulate identification, investigation, and corrective actions designed to assess, correct, and prevent the risk of visible particulate contamination. The draft guidance also clarifies that meeting an applicable U.S. Pharmacopeia (USP) compendial standard alone is not generally sufficient for meeting the current good manufacturing practice (CGMP) requirements for the manufacture of injectable products.

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2021-D-0241 for "Inspection of Injectable Products for Visible Particulates." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002; Office of Communication, Outreach and Development, Center for Biologics Evaluation and Research,

Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002; or the Policy and Regulations Staff (HFV-6), Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Eric Dong, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 75, Rm. 6652, Silver Spring, MD 20993-0002, 240-402-4172; Stephen Ripley, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911; or Laura Huffman, Center for Veterinary Medicine (HFV-140), Food and Drug Administration, Metro Park North 2 (MPN2), Rm. Hotel CVM, 7500 Standish Pl., Rockville, MD 20855, 240-402-0664.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Inspection of Injectable Products for Visible Particulates.” Visible particulates in injectable products can jeopardize patient safety. The draft guidance addresses a holistic approach to visible particulate control that incorporates risk assessment, prevention, inspection, identification, and remediation of visible particulates in injectable products.

Adherence to FDA’s CGMP requirements, as set forth in section 501 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 351) and 21 CFR parts 210 and 211 for drug, animal drug, and biological products; 21 CFR 600.10 through 600.15 for biological products; and 21 CFR part 4 for combination products, is essential for the control of visible particulates in injectable products. Adherence to compendial standards can also assist manufacturers in complying with CGMP requirements. USP General Chapter <1> *Injections and Implanted Drug*

Products (Parenterals)--Product Quality Tests states that “[t]he inspection process should be designed and qualified to ensure that every lot of all parenteral preparations is essentially free from visible particulates” as defined in USP General Chapter <790> *Visible Particulates in Injections*. Injectable products with a USP monograph are required to meet the applicable criteria from these USP General Chapters (see section 501(b) of the FD&C Act).

Noncompendial products should also be “essentially free from visible particulates” as defined in USP General Chapter <790>.

Applying acceptance criteria, such as the criterion outlined in USP General Chapter <790>, is an important component of the overall visible particulate control program, but meeting these acceptance criteria alone is not sufficient to ensure compliance with the applicable CGMP requirements identified above, which cover a broader array of manufacturing practices than product inspection. Full compliance with CGMP requirements is needed to ensure the continued supply of pure, safe, and effective injectable products.

This draft guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on “Inspection of Injectable Products for Visible Particulates.” It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information in 21 CFR parts 211, 314, and 601 have been approved under OMB control numbers 0910-0139, 0910-0001, and 0910-0308, respectively.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at

<https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs>,
<https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances>, <https://www.fda.gov/animal-veterinary/guidance-regulations/guidance-industry>, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>, or <https://www.regulations.gov>.

Dated: December 14, 2021.

Lauren K. Roth,

Associate Commissioner for Policy.

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